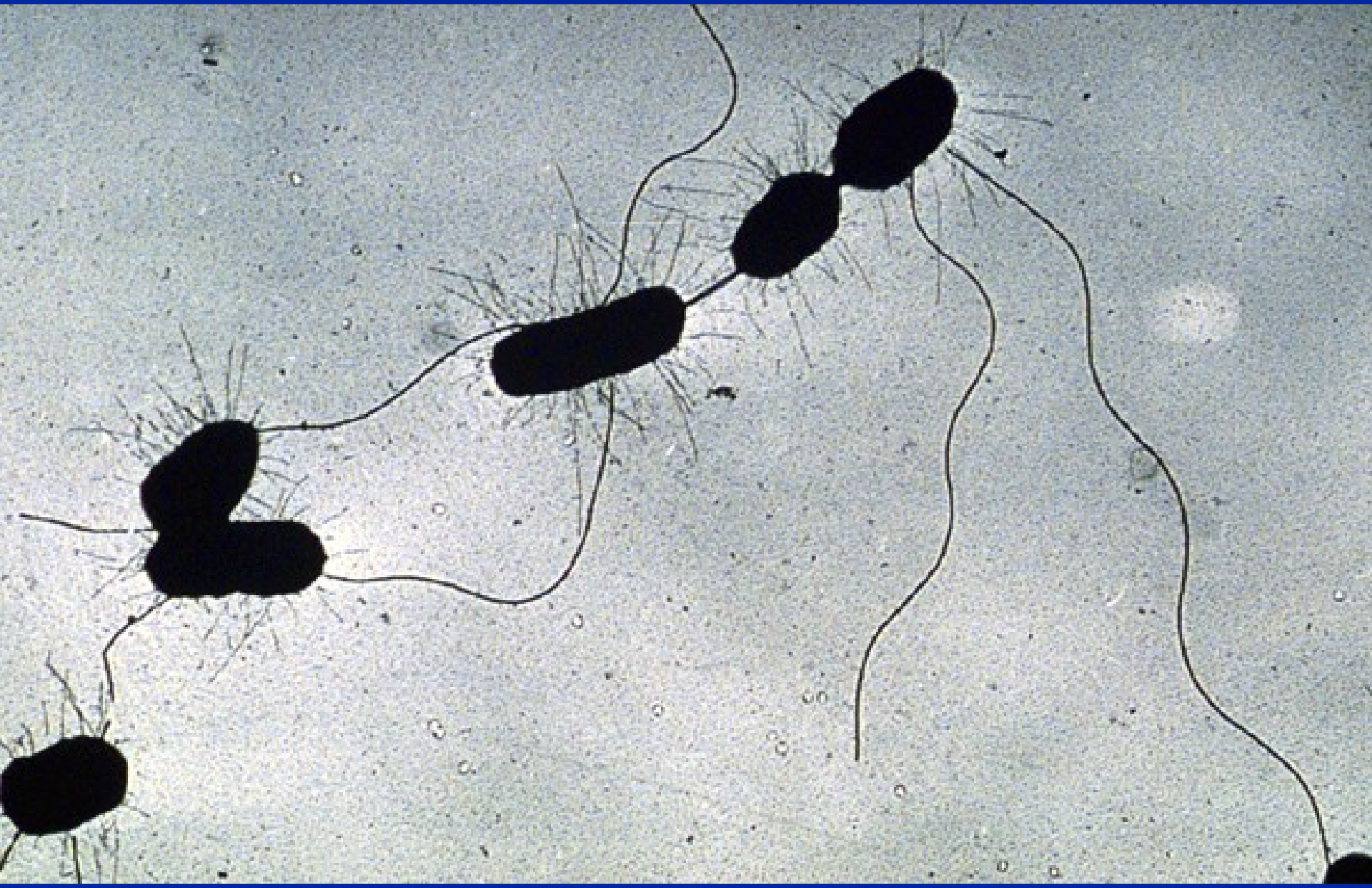
Emerging Infectious Diseases

Global Medicine 2005

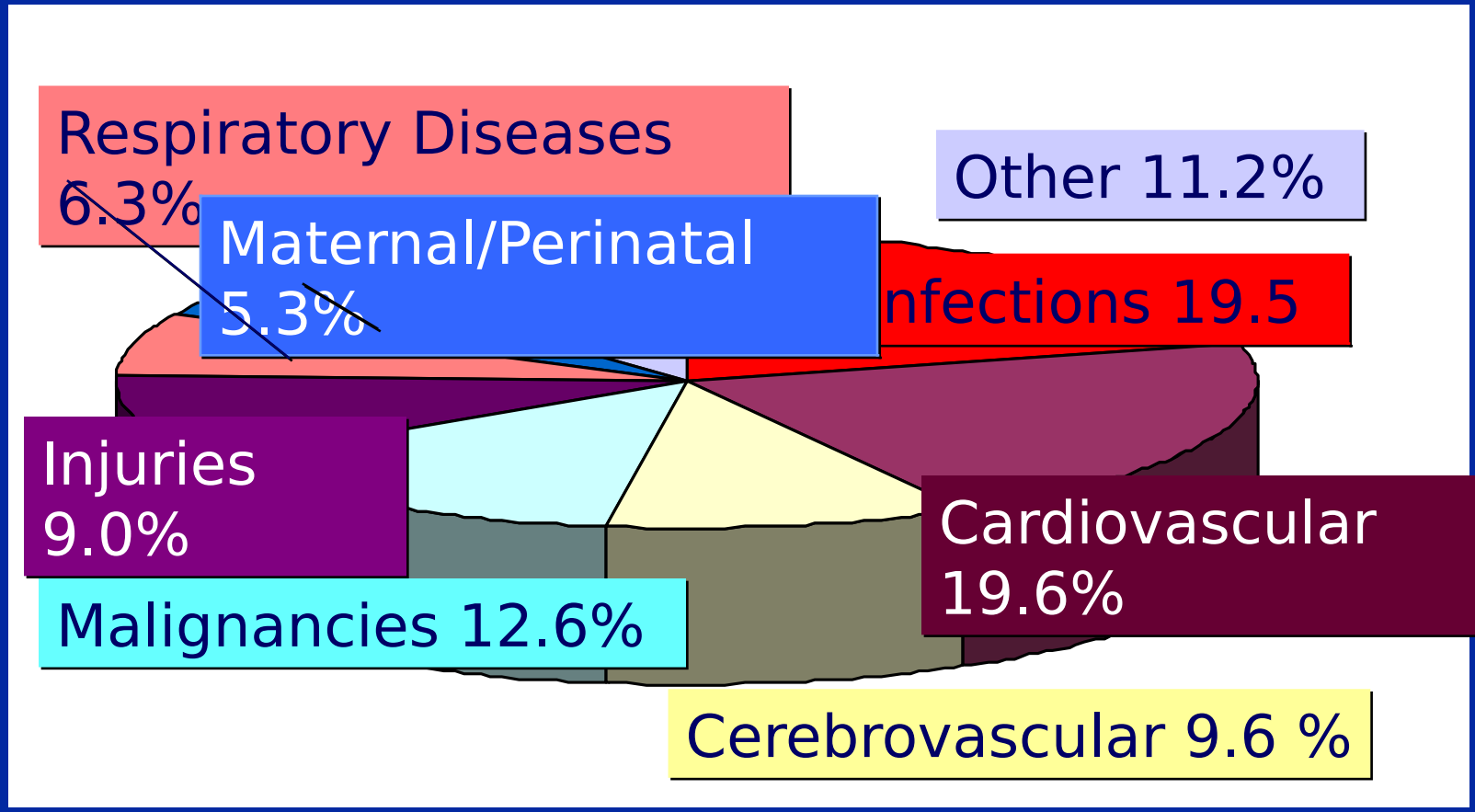
COL Ted Cieslak, MC, USA

Dept of Pediatrics

Brooke Army Medical Center



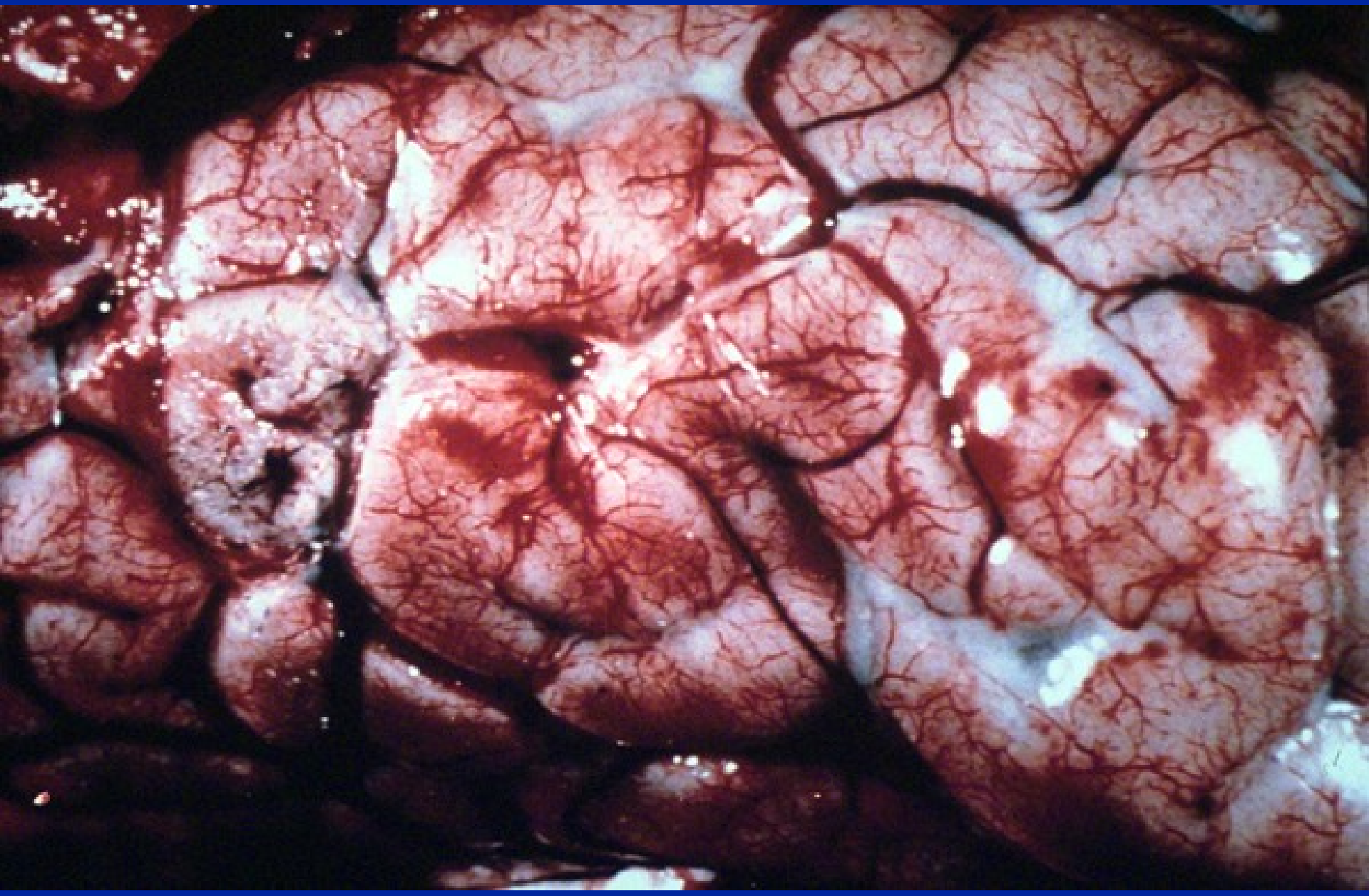
Causes of Death: 2002

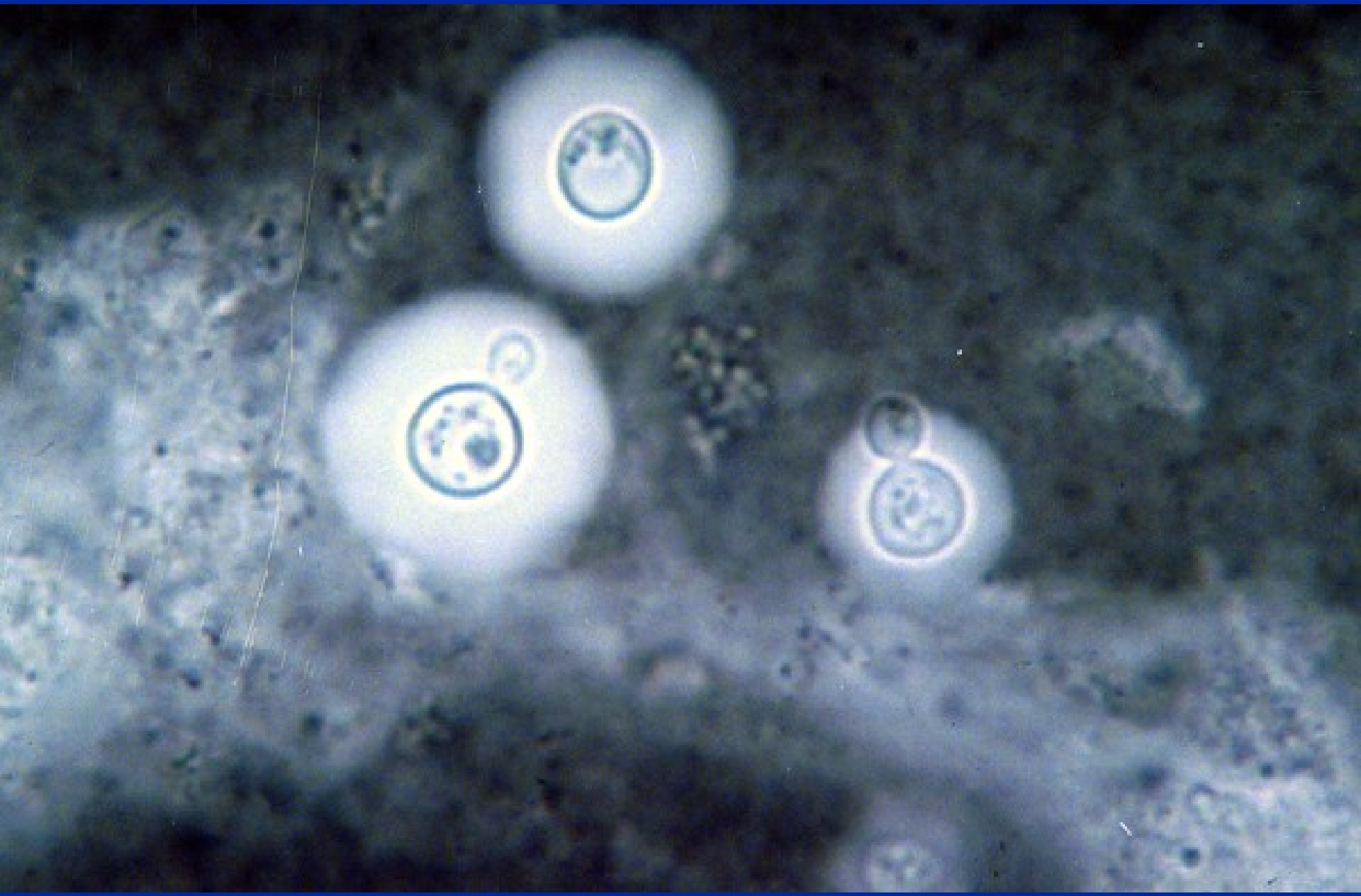


World Health Organization: *World Health Report 2003*

Leading Infectious Causes of Death 2002

- Lower respiratory inf. 3.8 million
- HIV/AIDS 2.8
- Diarrheal diseases 1.8
- Tuberculosis 1.6
- Malaria 1.2
- Measles 0.8
  - *World Health Organization, World Health Report, 2003*

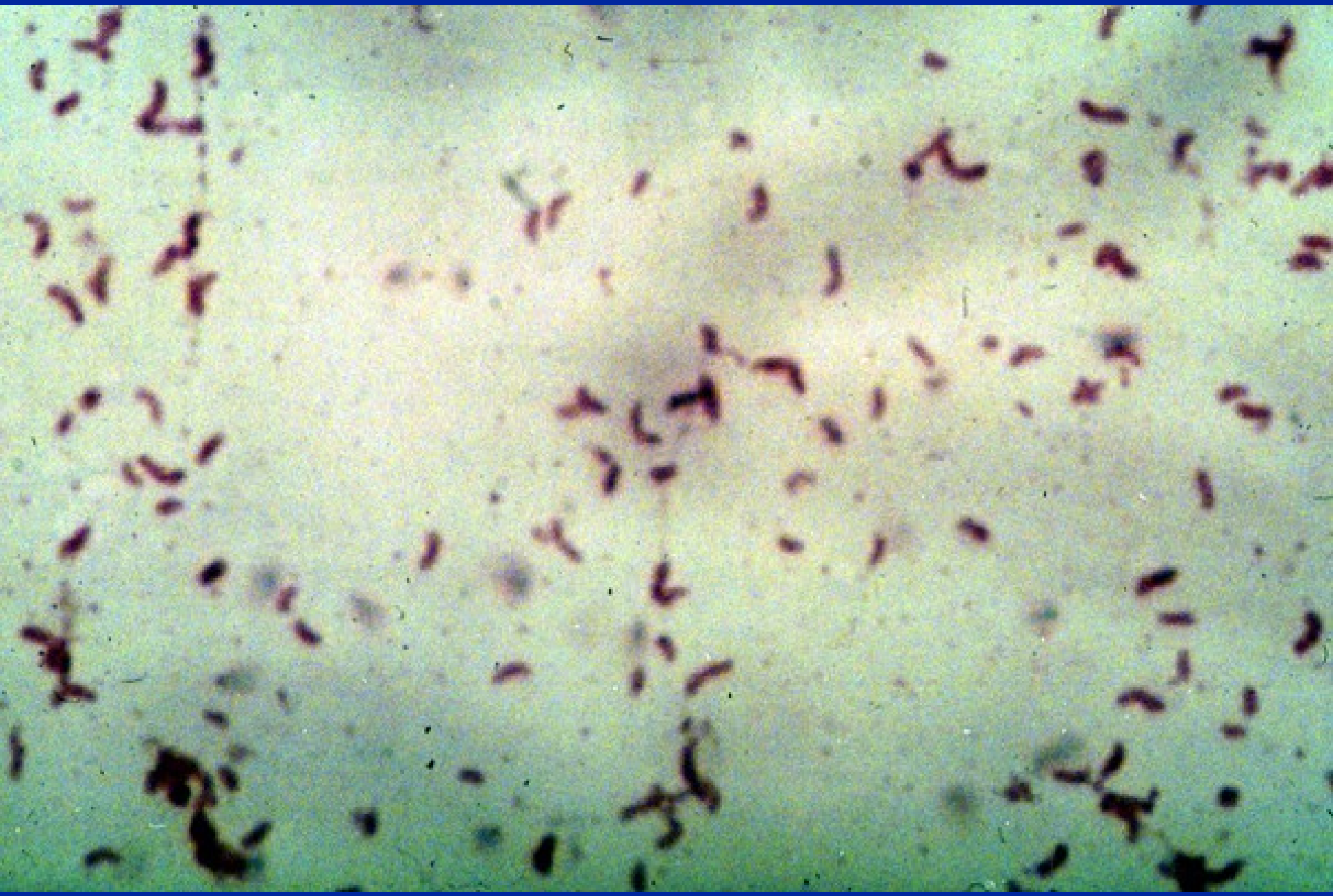




Emerging Infections

- Newly identified disease
- Increased incidence over past 2 decades
- Incidence expected to increase over next 2 decades

Courtesy of J. Brundage, Henry M. Jackson Foundation for the Advancement of Military Medicine, Rockville, MD



Ingredients for Emergence

- **Pathogen: Adaptation and Change**
  - **Virulence**
    - **Adherence**
    - **Invasiveness**
    - **Toxin production**
    - **Evasion of host immune defenses**
  - **Antibiotic Resistance**
  - **Expansion to new environments, reservoirs, vectors (“microbial traffic”)**

Gambian giant-pouched rat (*C. gambianus*)

courtesy Utah Hogle Zoo

Copywrite picture

Copywrite picture

Ingredients for Emergence

- Increased population at risk
  - Genetic predisposition
  - Co-infection
  - Urban migration and poverty
  - Crowding, poor hygiene
  - Impaired immunity
  - Inadequate public health infrastructure
    - Disease surveillance
    - Prevention programs
    - Trained personnel
      - Epidemiologists, scientists, rodent/vector control personnel, patient educators

Emergence of *Vibrio cholerae* O139 India, Bangladesh: 1992

Pathogen: ***Vibrio cholerae.***

Dynamic change: **O139 capsular antigen**

Reservoir: **Warm water (Ganges, Bay of Bengal); nutrients (fertilizer runoff, sewage)…supports algae…**

Dynamic change: ***Monsoon*****… flooding expands geographic range of O139**

Host: **Humans; high prevalence of *H. pylori*; poor sanitation/hygiene**

Dynamic change: **exposure to O139**

Population: **Crowding, degradation of sanitation, access to safe drinking water**

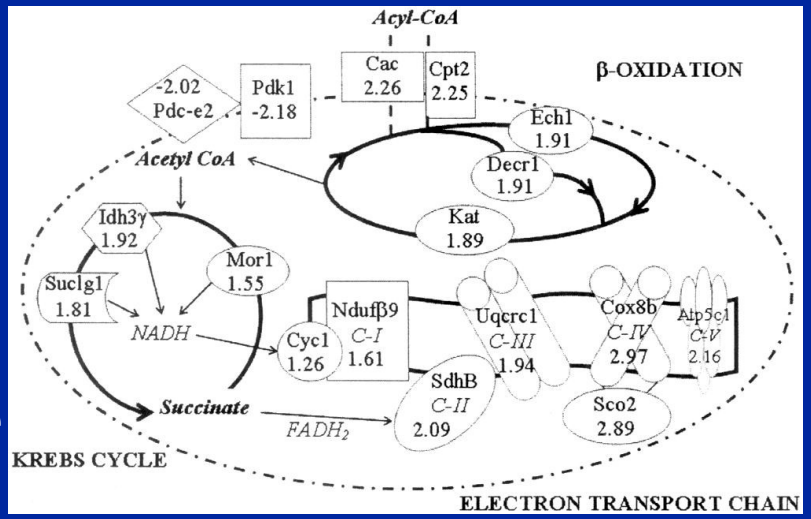
Dynamic change: **Social upheaval p monsoon flooding exacerbates crowding, degradation of sanitation, access to safe drinking water…**

What do

- Biochemical pathways
- Clotting cascade
- Pro-inflammatory cytokine cascade
- Emerging Diseases
- Avalanches
- Power outages

have in common???

Pathogen → Reservoir → Vector → Host → Population



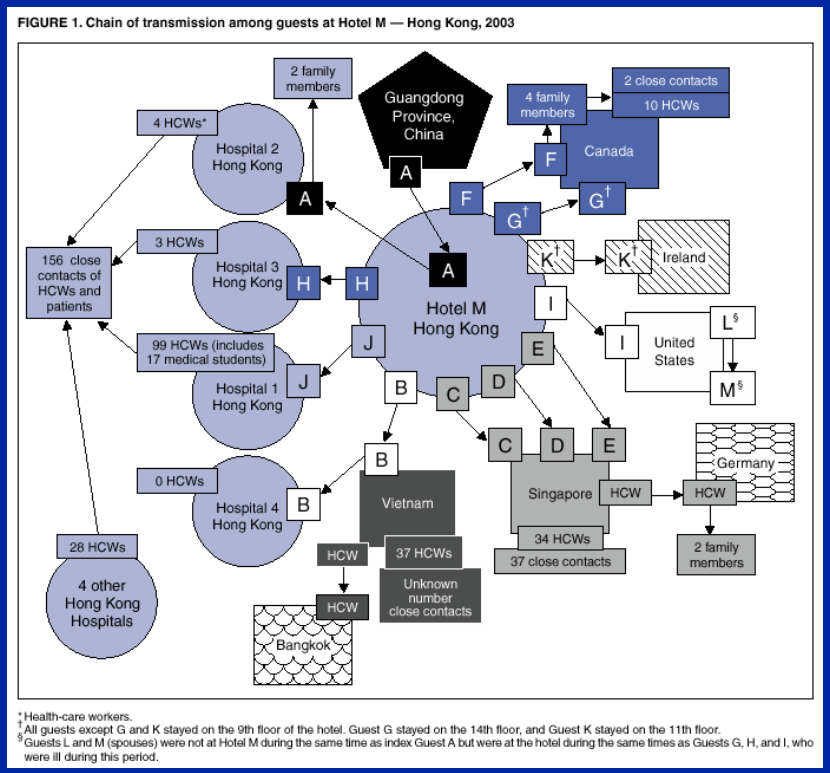


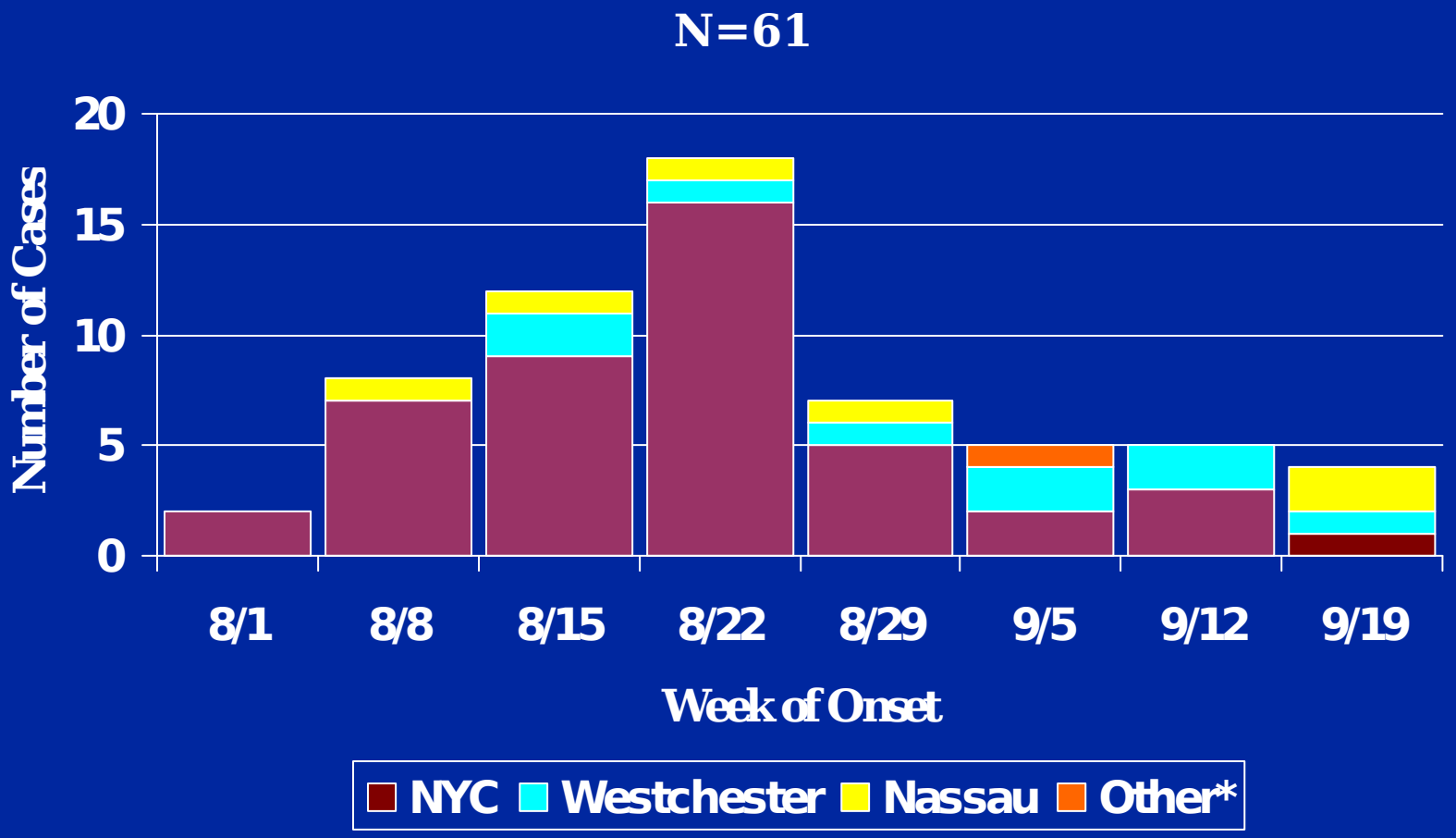
FIGURE 1. Chain of transmission among guests at Hotel M — Hong Kong, 2003
2 family members
Guangdong Province, China
4 family members
2 close contacts
10 HCWs
4 HCWs*
Hospital 2 Hong Kong
Canada
3 HCWs
156 close contacts of HCWs and patients
Hospital 3 Hong Kong
Hotel M Hong Kong
Ireland
United States
99 HCWs (includes 17 medical students)
Hospital 1 Hong Kong
0 HCWs
Hospital 4 Hong Kong
Vietnam
Singapore
HCW
Germany
34 HCWs
37 close contacts
2 family members
28 HCWs
4 other Hong Kong Hospitals
37 HCWs
Unknown number close contacts
Bangkok
* Health-care workers.
† All guests except G and K stayed on the 9th floor of the hotel. Guest G stayed on the 14th floor, and Guest K stayed on the 11th floor.
§ Guests L and M (spouses) were not at Hotel M during the same time as index Guest A but were at the hotel during the same times as Guests G, H, and I, who were ill during this period.

MMWR 2003;52:241-248

Encephalitis: NYC, 1999

- 23 Aug: 2 cases of encephalitis reported
  - NYCDOH identifies cluster of 6 patients
    - 5 :severe muscle weakness, axonal periph neuropathy
    - 4: required respiratory support
- 30 Aug: Active Surveillance
  - Presumptive viral encephalitis +/- muscle weakness, acute flaccid paralysis, GBS, aseptic meningitis after 1 Aug 99
- 3 Sept: Serologies:
  - IgM ELISA to common North American Arboviruses: St. Louis Encephalitis
- 3 Sept: Mosquito Control

Epidemic Encephalitis
New York State August-Sept 1999

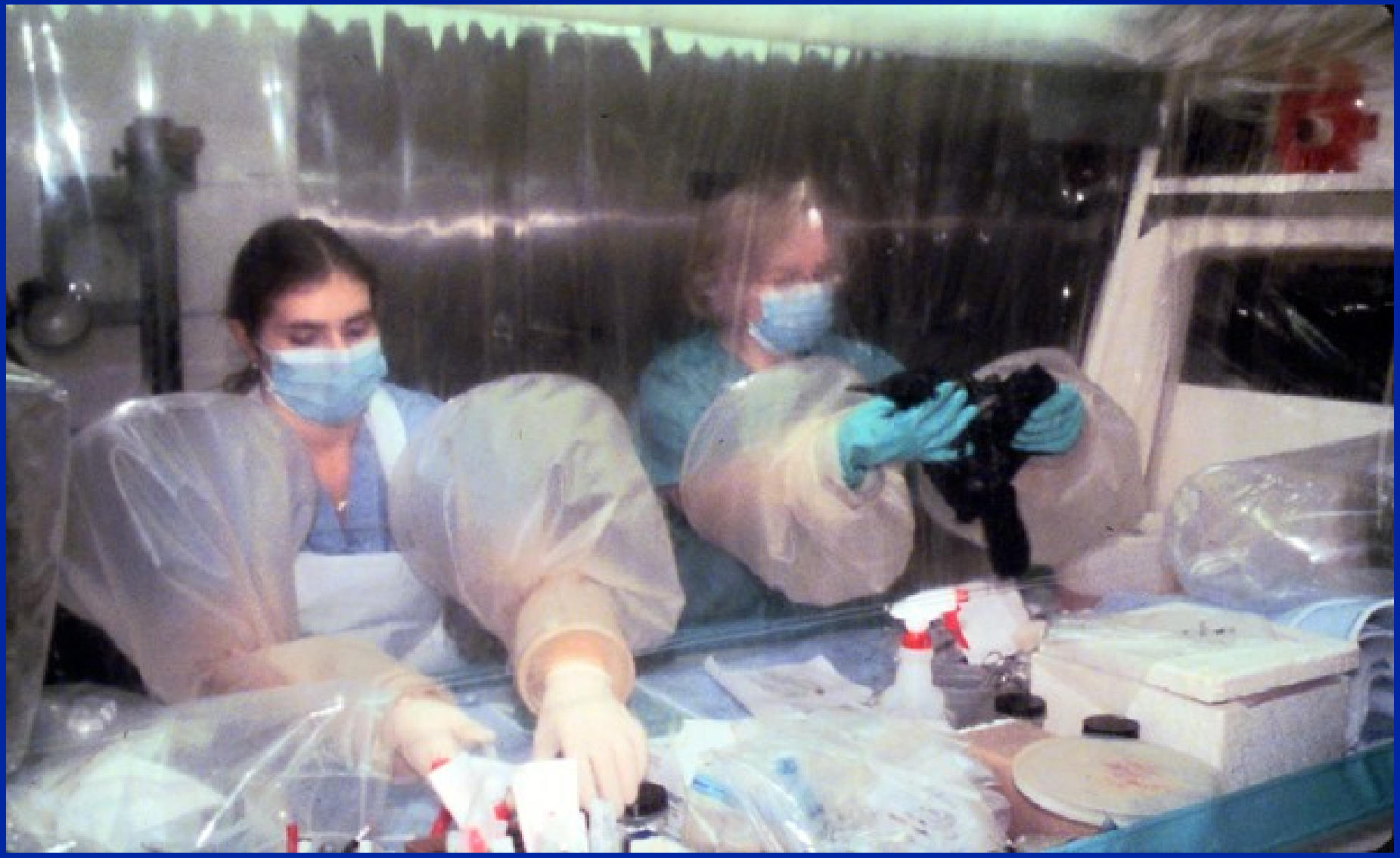


* Pt. lives in Toronto but has travel history to NYC

Epizootic: Birds, New York City

Vet Pathol 2000;37:208-24

- **June-July 1999: Unexplained bird “die-off”**
  - **Thousands of crows (*Corvus brachyrhynchos*) estimated to have died**
  - **Other species: mallard, blue jay, rock dove, robin, ring billed gull, laughing gull, sandhill crane**
- **10 Aug-23 Sept: Deaths among 27 rare exotic birds at Bronx and Queens Zoos**
  - **Bald Eagle**
  - **Asian pheasants**
  - **Guanay cormorants**
  - **Snowy Owl**
  - **Blythe’s tragopan**
  - **Night heron**
  - **Bronze winged ducks**
  - **Black-billed magpie**
  - **Chilean flamingoes**

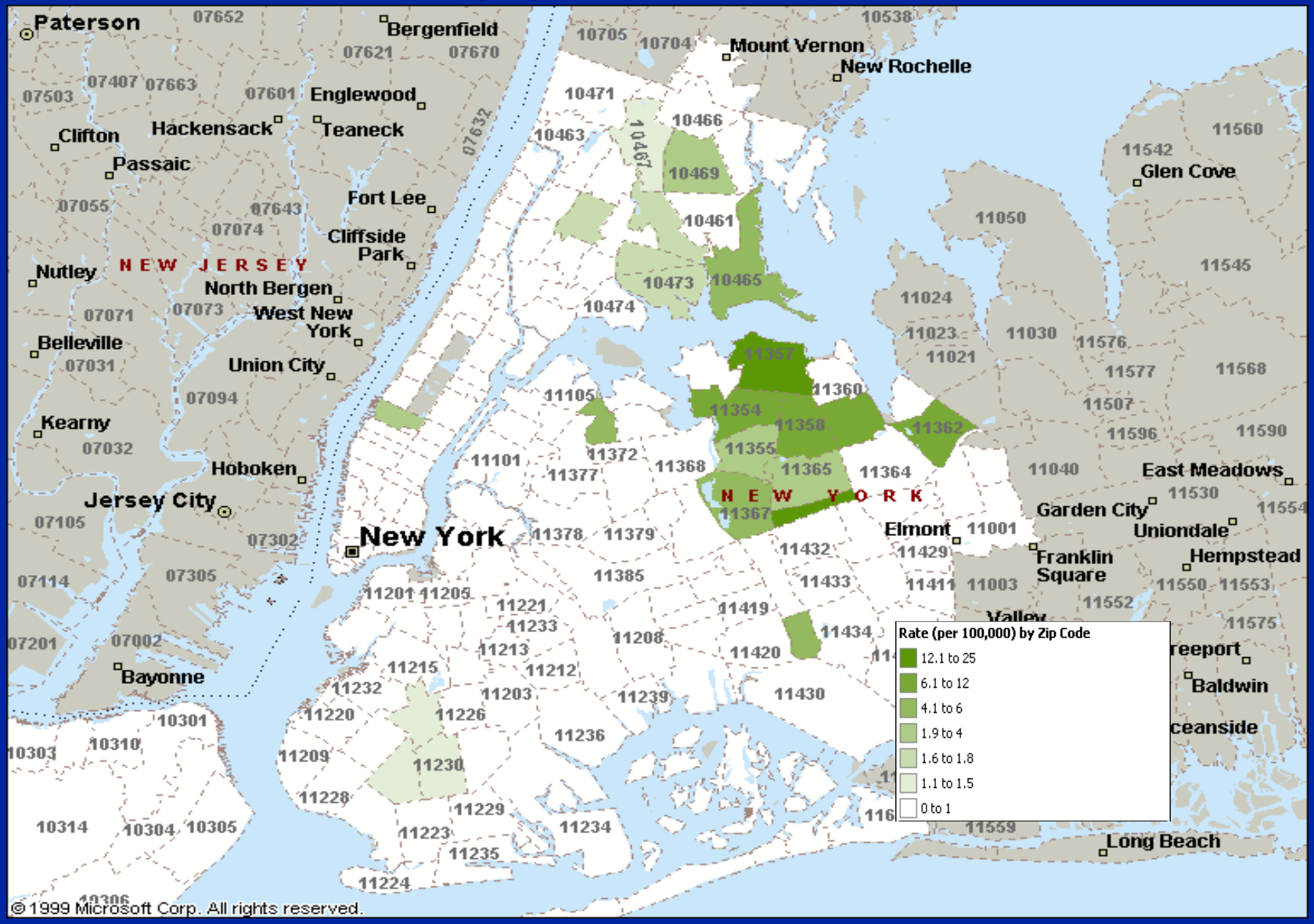


WCS
WILDLIFE CONSERVATION SOCIETY

St. Louis Encephalitis ?

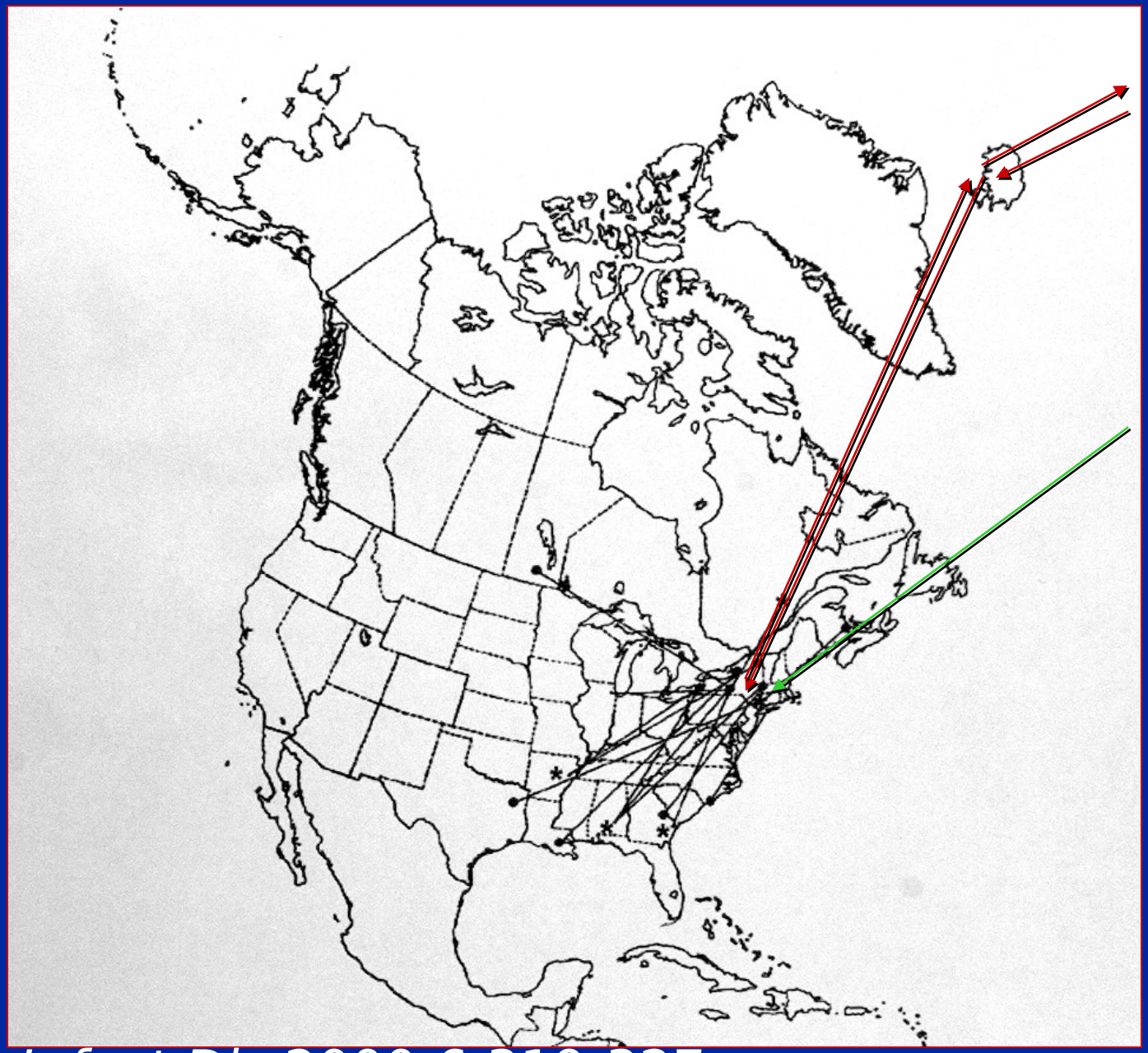
- 10 Sept: Bird tissues sent to USDA National Veterinary Services Laboratories
  - Tests for common avian pathogens and equine encephalitis viruses negative
- 23 Sept: WNV RNA identified in bird tissue by PCR
- WNV identified in human cases
  - PCR: Gene sequences identical to bird isolates
  - IgM: + in all SLE +, 10 borderlines and 8 negatives

Rates of clinical cases of West Nile Virus by zip code per 100,000 population, NYC 1999



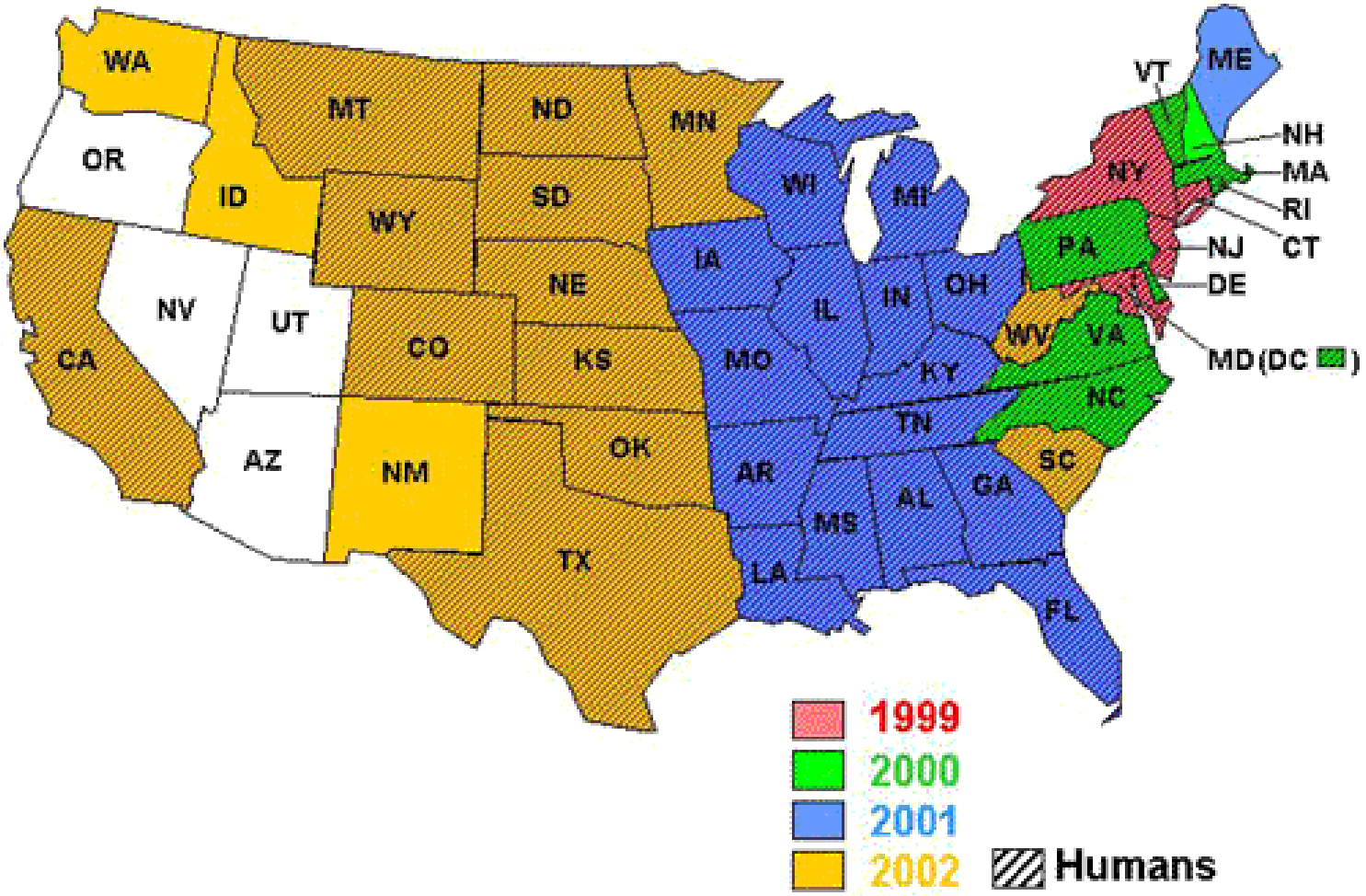
WNV

- **Mosquito-borne flavivirus**
  - Africa
  - Europe
- **Importation to Western Hemisphere**
  - Bird migration patterns?
  - Illegal traffic in exotic birds?
  - Imported mosquito vectors?
  - Imported human cases?
  - Bioterrorism attack?

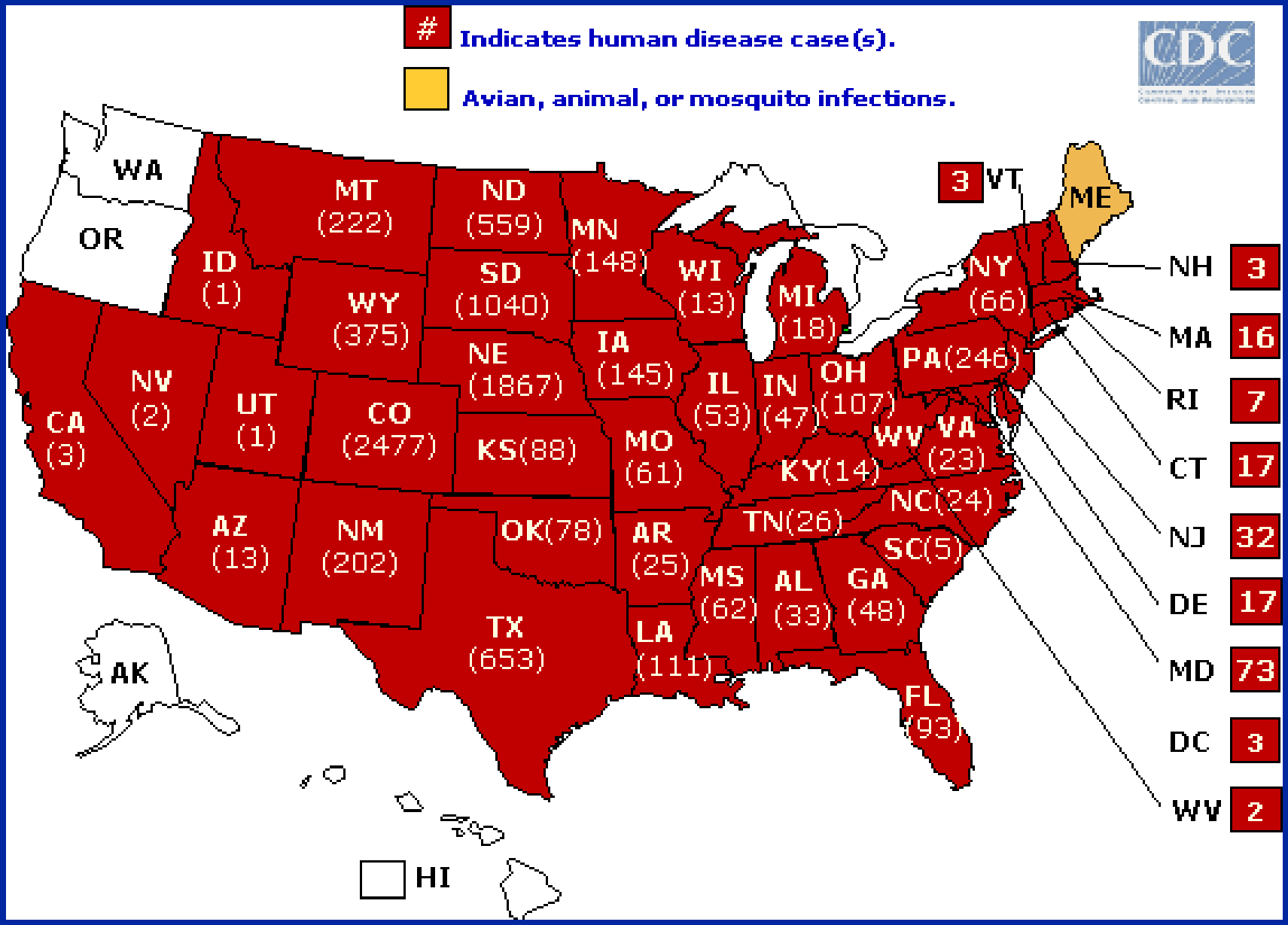


Emer Infect Dis 2000;6:319-327

West Nile Virus in the United States, 1999 - 2002



West Nile Virus: 2003



Emergence of West Nile: USA

Year	Cases	Deaths
1999	66	7
2000	21	2
2001	62	7
2002	4156	284
2003	9100	220

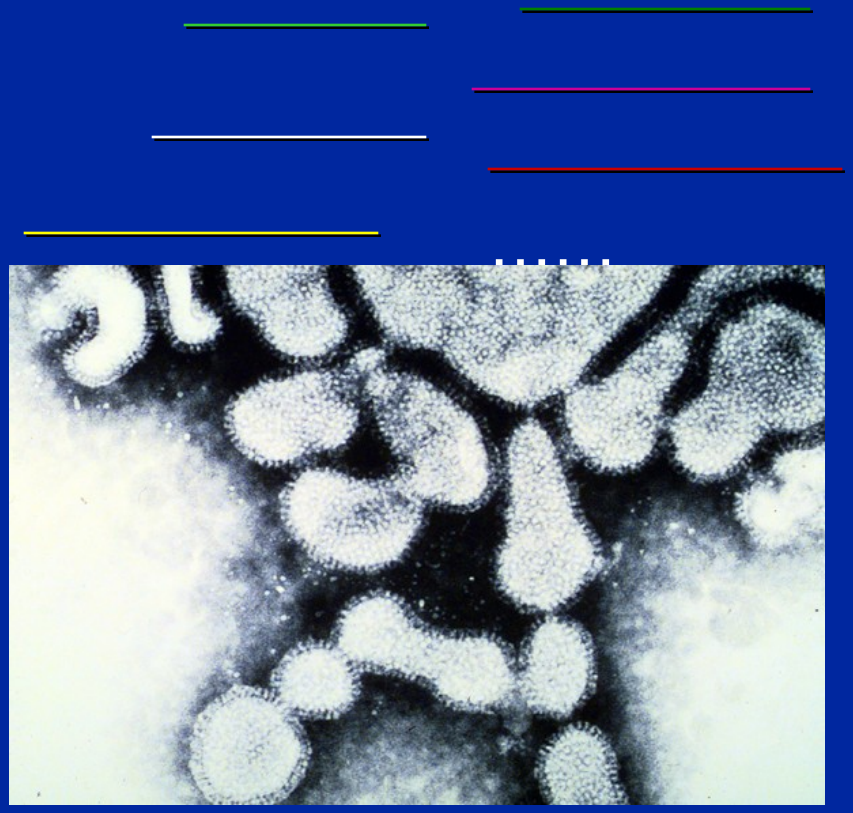
- Education: Avoidance of risk
  - Repellants
  - Long sleeves
- Mosquito control
- Vaccine??
- Treatment??

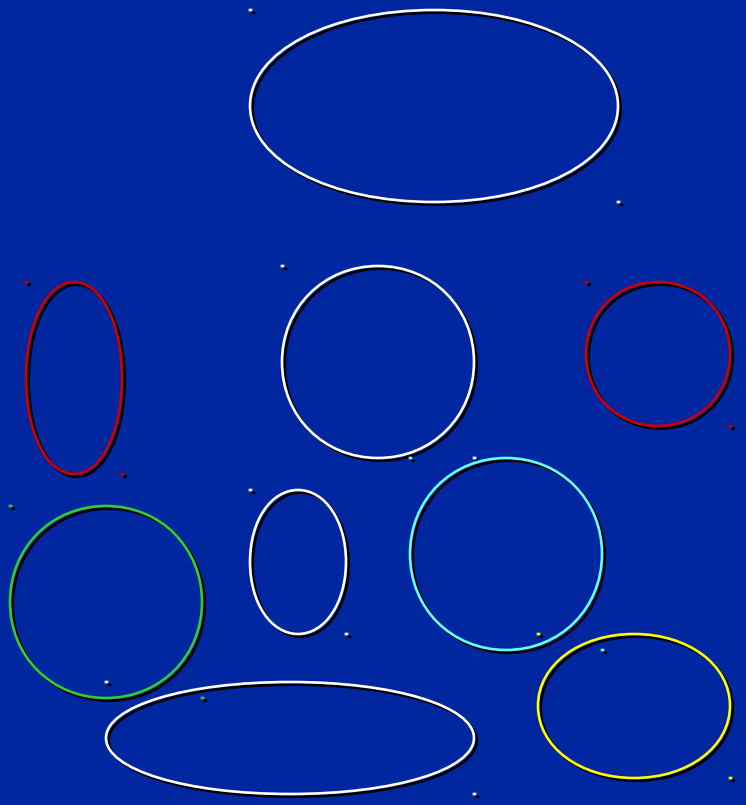
Influenza A: Shift vs Drift

Bird-human reassortments
1957 (H2N2) and 1968 (H3N2)

Hemaglutanin
At least 15 subtypes

Neuraminidase
At least 9 subtypes





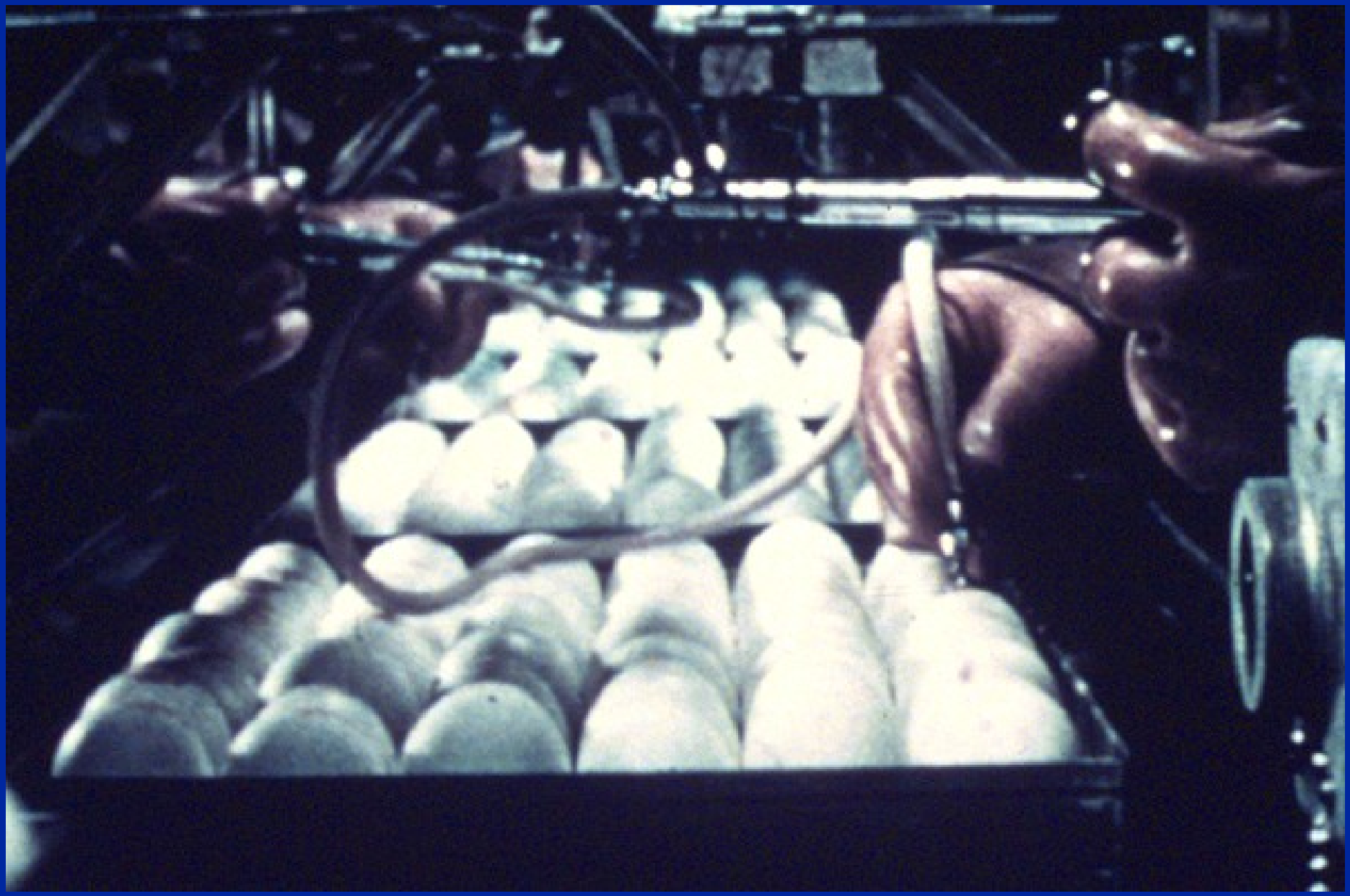
해충살물상회
지파

Influenza A H5N1 Hong Kong, 1997

- Reservoir: Ducks
- Emerged among chickens (70% fatality)
- Chickens served as amplifying host, reservoir for human disease
- 18 human cases, 6 deaths
- 1.6 million chickens slaughtered to eradicate reservoir of human disease
- Outbreak contained
- Active surveillance of Chinese poultry farms for H5N1; new licensing standards for poultry industry
- Chickens quarantined in holding farms for 5 days prior to shipment to Hong Kong

Influenza A H5N1 Hong Kong, 1997

- Slaughter of chickens completed shortly before arrival of influenza A H3N2 Sydney
- Implications: if strains had co-circulated, possible genetic resortment-? virulent strain transmissible to humans?
- Pandemic influenza
  - Ability to replicate in humans
  - Transmissible person-to-person
  - Susceptible population



Re-Emergence of "Bird Flu"

- H5N1: February 2003
  - Three cases, two deaths
  - Residents of Hong Kong; had traveled to Fujian Province
- H5N1: Dec 2003
  - Epizootic: Chickens: Japan, S Korea, Vietnam, Thailand, Pakistan, Indonesia, Laos, Cambodia, China
  - Human cases and deaths: Vietnam, Thailand: 23 cases, 18 deaths
  - Antigenic drift
    - 1997 Hong Kong, 2003 S Korea, Vietnam
  - Antiviral resistance: Vietnam, Thailand: amantadine, rimantadine

- H7N7: February-March 2003
  - Poultry: Belgium, Netherlands
  - 87 human cases; one death in Netherlands
- H7N?: USA 2004

Monkeypox: Democratic Republic of Congo Feb 1996-Oct 1997

- 88 cases in 12 villages (ages 1 mo-62 yrs; median age 10 yo (50% 5-19)
- Attack Rate by Age (Akungula)
  - < 15 yo: 146/1000
  - 15-24 yo: 47/1000
  - > 24 yo: 73/1000
- Vaccination scar: 15%
- Secondary attack rate 8%
- Case fatality rate 3.7%

Hutin et al. *Emerg Inf Dis* 2001;7:438-434

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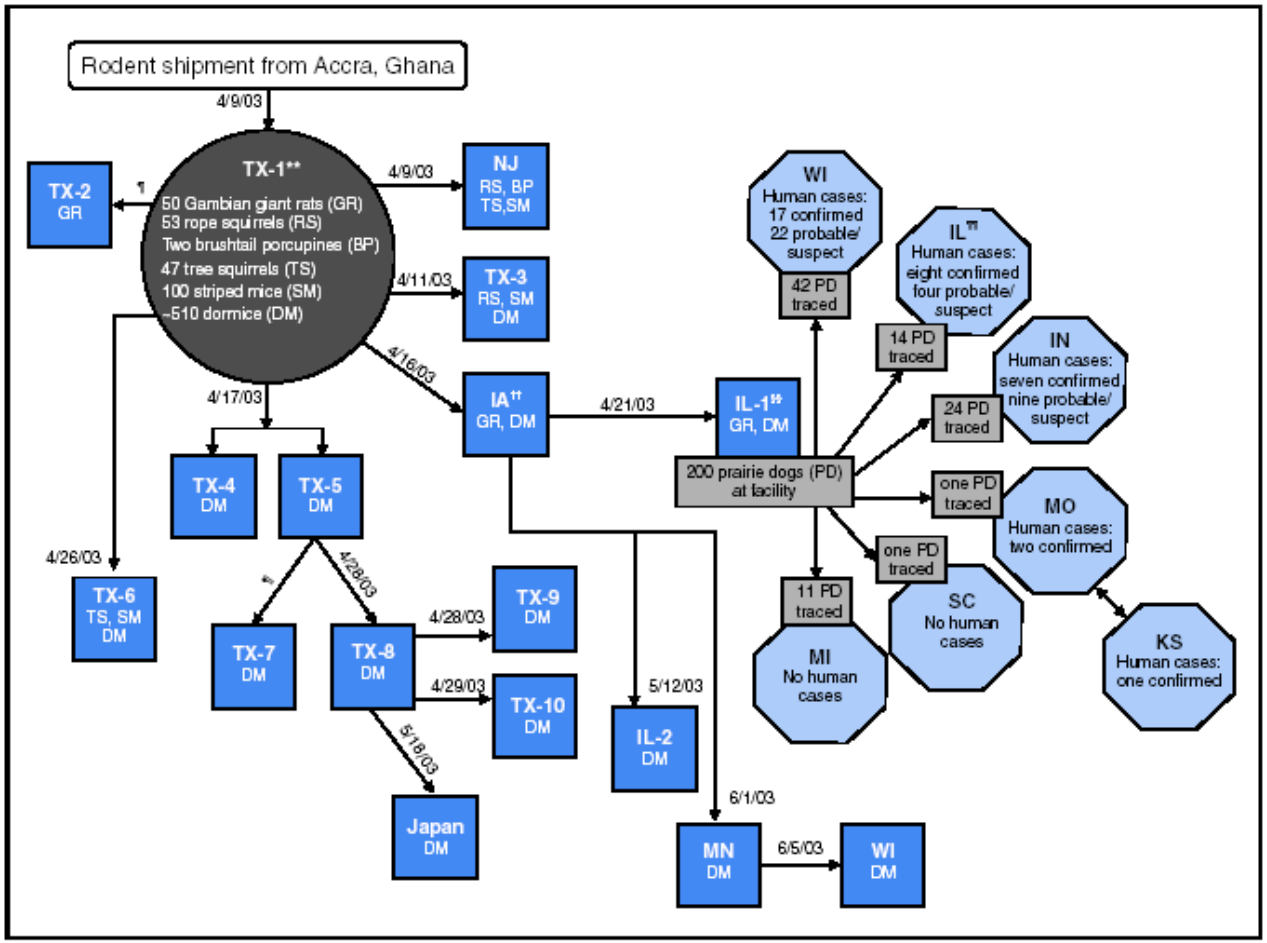
Gambian giant-pouched rat (*C. gambianus*)

courtesy Lincoln Park Zoo

courtesy APHIS USDA

Here comes trouble...

FIGURE 2. Movement of imported African rodents to animal distributors and distribution of prairie dogs from an animal distributor associated with human cases of monkeypox — 11 states*, 2003†§



* Illinois (IL), Indiana (IN), Iowa (IA), Kansas (KS), Michigan (MI), Minnesota (MN), Missouri (MO), New Jersey (NJ), South Carolina (SC), Texas (TX), and Wisconsin (WI). Japan is included among sites having received shipment of rodents implicated in this outbreak.
† As of July 8, 2003.
§ Does not include one probable human case from Ohio; investigation is ongoing.
¶ Date of shipment unknown.
** Identified as distributor C in *MMWR* 2003;52:561–4.
†† Identified as distributor D in *MMWR* 2003;52:561–4.
§§ Identified as distributor B in *MMWR* 2003;52:561–4.
¶¶ Includes two persons who were employees at IL-1.

MMWR 2003;52:642-646

Epidemiology of Monkeypox USA 2003
Laboratory Proven Cases (n = 35)

Characteristic	Number	%
Age (years)		
6-18	11	31
19-51	24	69
Gender		
Female	18	51
Male	17	49
Exposure		
Prairie dog(s) (PDs)	14	40
PDs + human cases (HC)	14	40
Premises housing PDs	6	17
Premises housing PDs + HC	1	3

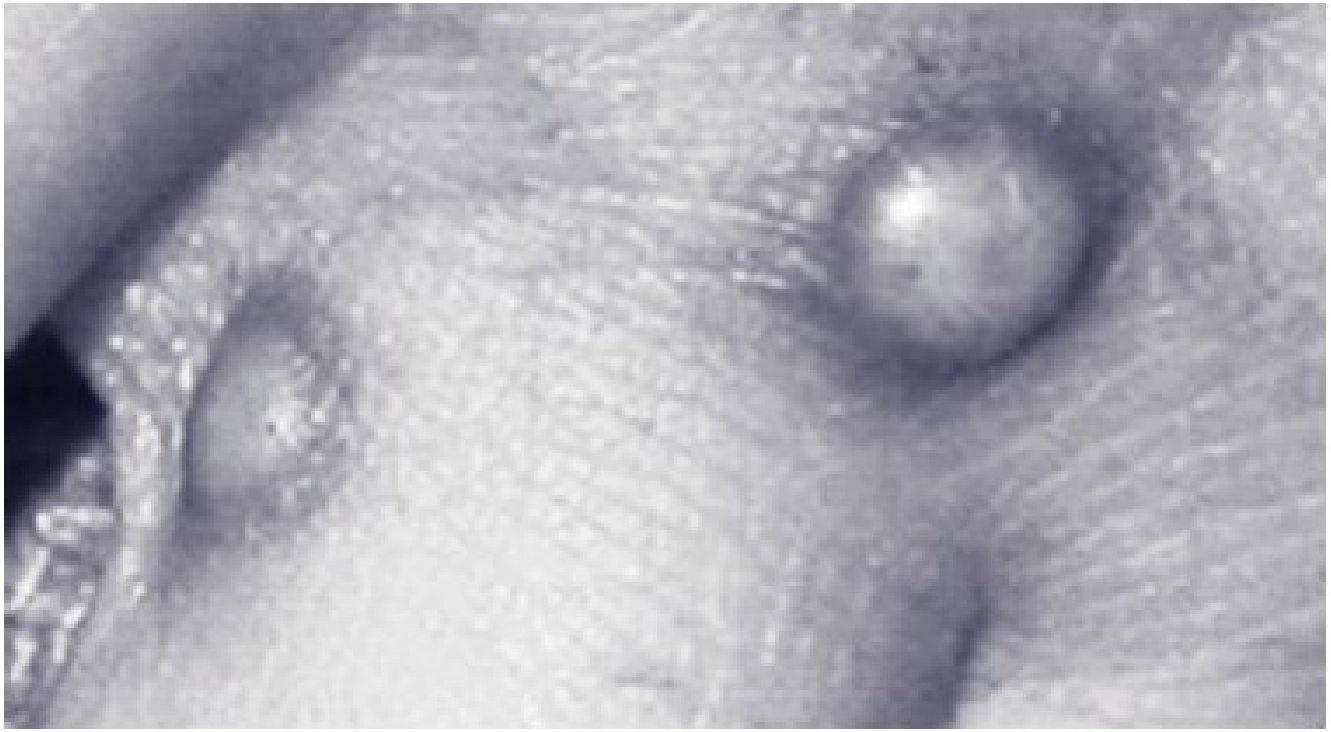
MMWR 2003;52:642-646

Clinical Features of Monkeypox USA 2003
Laboratory Proven Cases (n = 35)

Characteristic	Number	%
Rash	34	97
Fever	34	85
Resp Sxs	27	77
Lymphadenopathy	24	69
Hospitalized	16	46
Prev vaccinia	8	33

MMWR 2003;52:642-646

FIGURE 2. Secondary lesions of monkeypox on a patient's hand — Marshfield Clinic, Marshfield, Wisconsin, 2003



MMWR 2003; 52:537-40

Monkeypox: Response

- Outbreak investigation
  - Identification of risk groups
  - Active surveillance of risk groups
- Pre/post-exposure vaccination
  - Animal control workers, public health workers investigating animal or human cases
  - HCWs involved/may be involved in care of pts
  - Veterinary HCWs, animal caretakers, pet shop personnel caring for infected animals within p 4-14 days
  - Contacts of cases (4-14 days)
  - Lab workers handling specimens containing monkeypox virus
- Patient care
  - Isolation
  - Treatment
- Quarantine/euthanasia of animals
  - 178 of 762 African rodents imported 9 April “lost to followup”
- Outlaw sale of prairie dogs
- Outlaw importation of exotic rodents
  - Pets, food items

(*MMWR* 2003;57:642-646)

Atypical Pneumonia in China

- 10 Feb 2003
  - Epidemic of atypical pneumonia since Nov 2002
    - 305 Cases of life-threatening respiratory disease
    - Prevalent among HCWs and household contacts
    - No identifiable cause
- 18 Feb: Two cases of Influenza A H5N1, one death; had traveled to Fujian Province; 3d family member dies in Fujian
- 21 Feb 2003
  - Physician from Guandong Province visits Hong Kong
- 26 Feb
  - Physician hospitalized c severe atypical pneumonia
- 28 Feb
  - American businessman hospitalized in Hanoi c atypical pneumonia after arriving from Hong Kong
- 4 March
    - Physician from Guandong Province Dies
- 10 March
    - 18 HCWs from Prince of Wales Hospital report illness
    - Active surveillance: Telephone contct: > 50 additional cases

Atypical Pneumonia: China

- 12 Mar
  - WHO issues global alert re nosocomial epidemics of atypical pneumonia in Hong Kong and Hanoi
- 15 Mar
  - Cases in Singapore and Toronto; WHO issues emergency travel advisory
- 11-25 Mar
  - 156 pts hospitalized; 112 secondary, 26 teriary cases; 69 HCWs, 53 pts from index ward, 16 household contacts
- 18 Mar
  - Paramyxovirus identified as possible etiologic agent
- 20 Mar
  - Hong Kong health ministry trace 80% of cases to index case
- 27 Mar
  - WHO urges stringent screening of air travelers leaving affected areas

A Major Outbreak of Severe Acute Respiratory Syndrome in Hong Kong

Lee N, Hui D, Wu A, et al. New Engl J Med 2003;348:1986-94

N = 138

Incubation period 2-16 (median 6) days

Fever	100%	WBC < 3,500	33.9%
Chills/rigor	73.2	ALC < 1,000	69.6
Myalgia	60.9	Atypical L	15.2
Cough	57.3	Plts < 150,000	44.8
Headache	55.8	APPT > 38 sec	42.8
Dizziness	42.8	Elevated D-dimer	45.0
Sputum prod	29.0	Elevated ALT	23.4
Sore throat	23.2	Elevated CPK	32.1
Coryza	22.5	Elevated LDH	71.0
N/V	19.6	Hyponatremia	20.3

Clinical Outcome

New Engl J Med 2003;348:1986-94

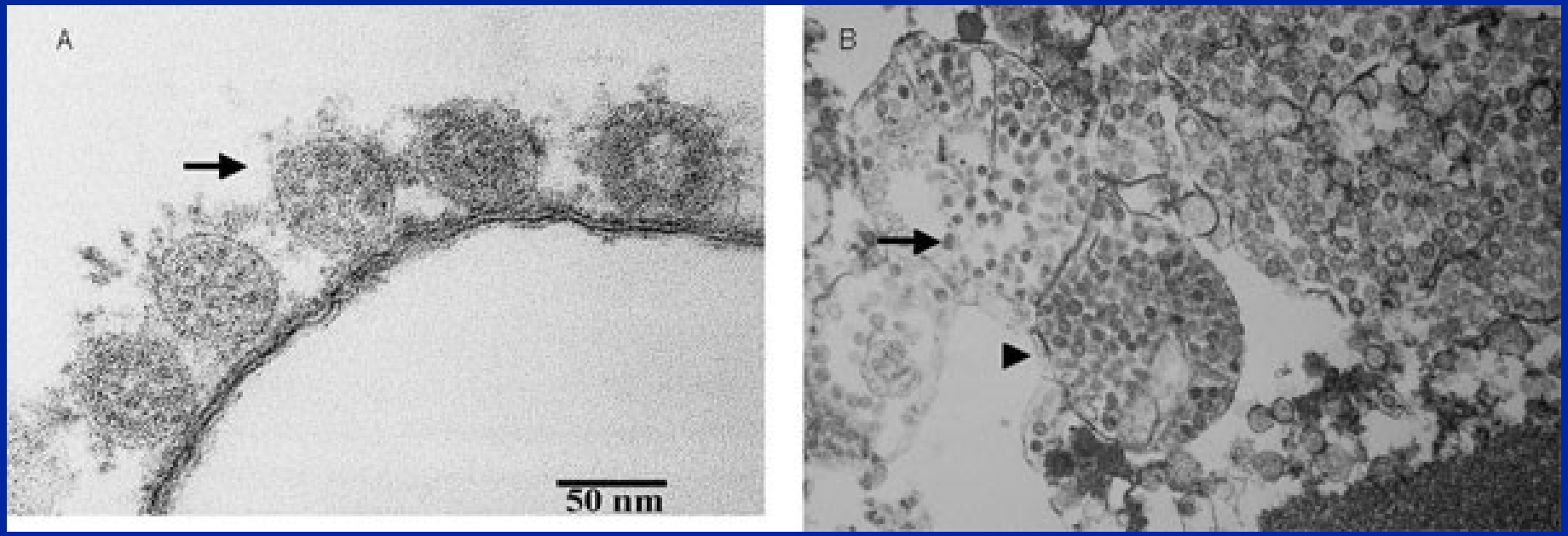
Admitted to ICU 23.2%

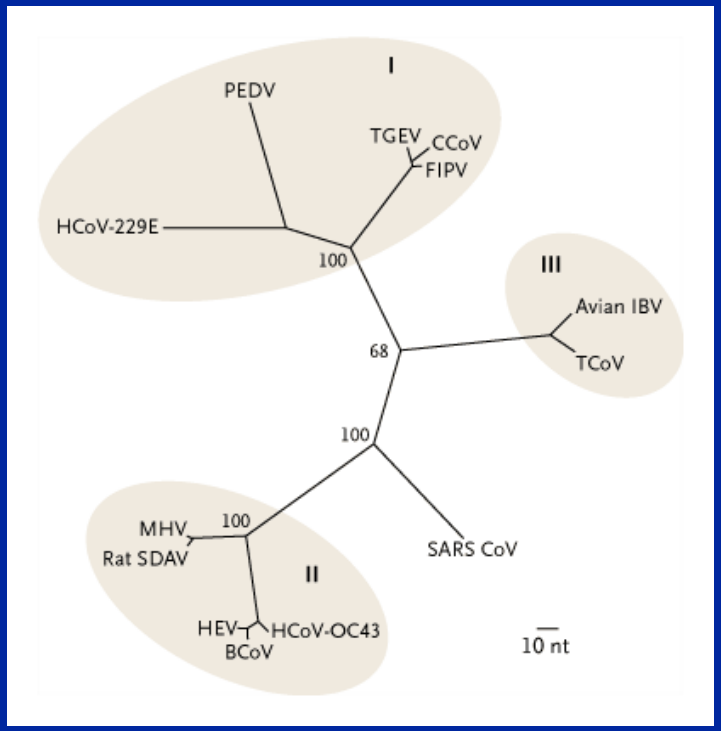
Mechanical vent 13.8

Death 3.6

Associated c ICU care or death by multivariate analysis:

- **Age (OR 1.80 95% CI 1.16-2.81 P = 0.009)**
- **High LDH (OR 2.09 for each 100 U P= 0.03)**
- **Elevated PMN on presentation (OR 1.60, P = 0.04)**





Phylogeny of SARS Coronavirus

New Engl J Med 2003;348:1953-66

SARS-CoV: Animal Reservoirs?

- Masked palm civet
- Racoon dog
- Chinese ferret bad
- Wild pigs
- Macaque
- Fruit bats
- Snakes

Differ from human isolates: additional 29 nucleotide sequence

Seroprevalence: SARS-CoV Guandong Province, China

Occupation	Seroprevalence	
Wild animal traders	8/20	40%
Wild animal butchers	3/15	20%
Vegetable traders	1/20	5%

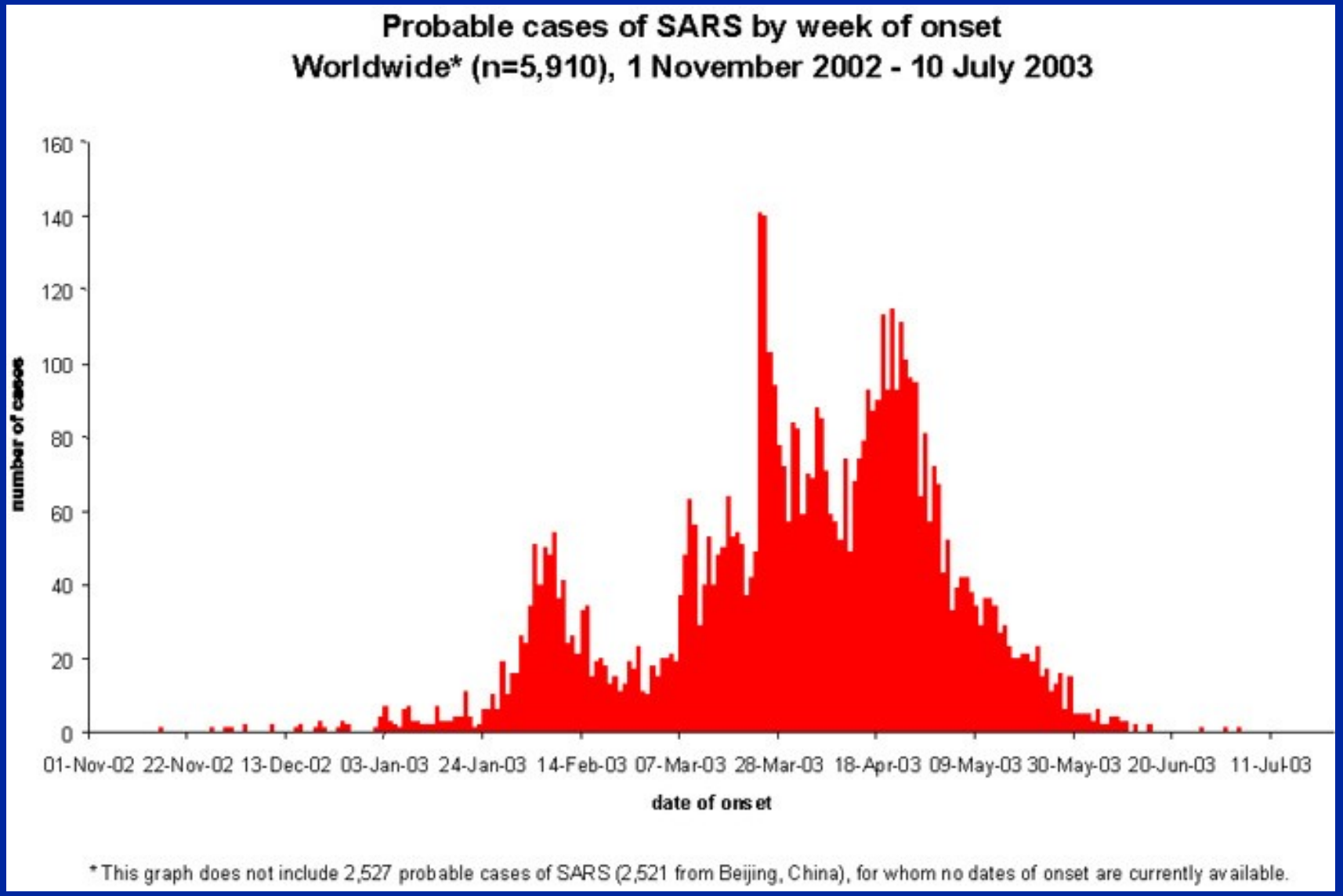
None had Sxs/Sxs SARS within preceding 6 months

"As a precautionary measure, persons who might come into contact with these species or their products, including body fluids and excretions, should be aware of the possible health risks, particularly during close contact such as handling and slaughtering and possibly food processing and consumption"

WHO 2003: Consensus Document on Epidemiology of SARS

Super-Spreading Events

- Aerosol generation
  - Nosocomial
    - Aerosol generation
      - Nebulizer treatments
      - Endotracheal intubation
      - Endotracheal suctioning
    - Delay: Transmission based precautions
  - Environmental aerosols
    - Amoy Gardens
- Ventilation
  - Taxicabs, aircraft



WHO 2003: Consensus Document on Epidemiology of SARS

SARS Response

- Construct case definition: Identify cases
  - Clinical
  - Epidemiologic
  - Lab
- Identify contacts
  - Active surveillance
  - Voluntary quarantine during incubation period
  - Travel restrictions
- Airport Screening
- Isolation/quarantine of case

SARS Case Definition: Clinical Criteria

- **Early Illness**
  - **Two or more of: subjective fever, chills, rigors, myalgia, headache, diarrhea, sore throat, or rhinorrhea**
- **Mild/moderate:**
  - **T > 100.4° F (38° C) and one or more findings of lower respiratory tract disease (cough, dyspnea)**
- **Severe:**
  - **Meets clinical criteria of mild/moderate illness and:**
    - **Radiographic evidence of pneumonia**
    - **ARDS**
    - **Autopsy findings c/w pneumonia or ARDS s identifiable cause**

SARS Case Definition: Epidemiologic Criteria

- **Possible exposure:**
  - **One or more within 10 days of onset of symptoms:**
    - **Travel to foreign or domestic location with documented or suspected recent transmission of SARS-CoV**
    - **Close contact with a person c mild to moderate or severe illness and history of travel in the 10 days before onset of symptoms to a foreign or domestic location with documented or suspected recent transmission of SARS-CoV**
- **Likely exposure:**
  - **One or more within 10 days of onset of symptoms**
    - **Close contact with a person c confirmed SARS-CoV**
    - **Close contact with a person with mild/moderate or severe illness c chain of transmission to confirmed case SARS-CoV in 10 days before onset of symptoms**

SARS Case Definition: Lab

- **Laboratory Criteria**
  - Detection of antibody to SARS-CoV by validated test
  - Isolation in cell culture of SARS-CoV from clinical specimen
  - Detection of SARS-CoV RNA by RT-PCR validated test and subsequent confirmation at a reference laboratory.
- **Exclusion Criteria**
  - Alternative diagnosis
  - SARS-CoV antibody negative at 28 days
  - Case reported on basis of contact with a person who was excluded; provided other epidemiologic or laboratory criteria are absent

Infection Control

- **Outpatient**
  - **Patient: Wear surgical mask**
    - **If not available, pt should cover mouth with disposable tissure when coughing, talking or sneezing. Separate pt from others in reception area**
  - **HCWs**
    - **should wear N-95 masks + Contact precautions + eye protection while caring for SARS suspects**
- **Inpatient**
  - **Standard + Contact + Airborne**
    - **Include Eye protection**
    - **If negative airflow room not available, use private room + N-95 mask**
    - **If N-95 masks not available, use surgical masks**

Active Surveillance

- **Unprotected high risk exposure**
  - **Dismiss from clinical duties for 10 days from last exposure**
  - **No restriction of activity outside of health care setting**
- **Symptomatic contact**
  - **Warn HC facility before presenting for evaluation**
  - **Mild illness: Confine to home**
  - **Mod-severe illness: Hospitalize under isolation**

SARS at Home

- **Case:**
  - **Restrict activities to home for 10 days following resolution of fever**
  - **Cover mouth with disposable tissue paper during coughing, sneezing**
  - **Surgical mask**
    - **(if unable to wear mask, household members to wear mask while caring for pt)**
  - **Hand hygiene**
- **Contact**
  - **Active surviellance**
- **Fomites:**
    - **Do not share eating utensils, bedding, towels until routine cleaning**

Encephalitis Malaysia, Sept 1998-April 99

- Pigs die of encephalitis and acute respiratory disease
- Pig farmers develop acute encephalitis
  - 265 cases, 105 deaths
- Japanese encephalitis suspected
  - Endemic mosquito-borne disease
  - Affects pigs and humans
- March 99: Epidemic encephalitis: Singapore

Nipah Virus Malaysia, Singapore: 1998-9

Nipah virus identified: new paramyxovirus

- **Reservoir: Fruit bats**
- **Transmission from pigs to humans:**
  - **Blood and body fluids**
- **Control Measures**
  - **Surveillance: Detect and cull infected herds**
  - **Destruction of 890,000 pigs**
  - **Ban on transporting pigs**
  - **Education**
    - **Standard precautions, protective equipment while working with pigs**
  - **Potential vaccine?**

What do *responses* to

- *E coli* 0157:H7
- Avian influenza
- SARS
- Monkeypox….

have in common???

Microbiology

Ecology

Meteorology

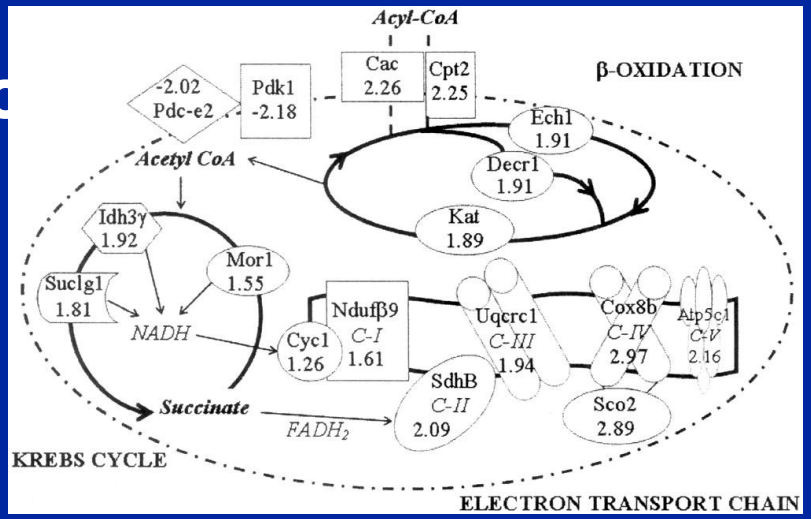
Entomology

Medicine

Immunology

Sociology

Public Health



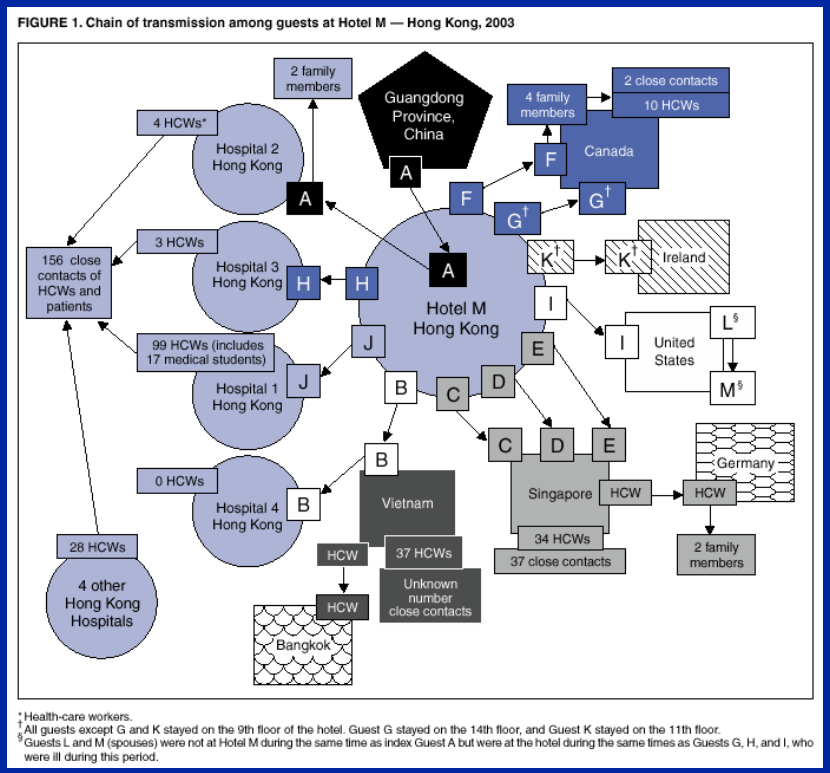
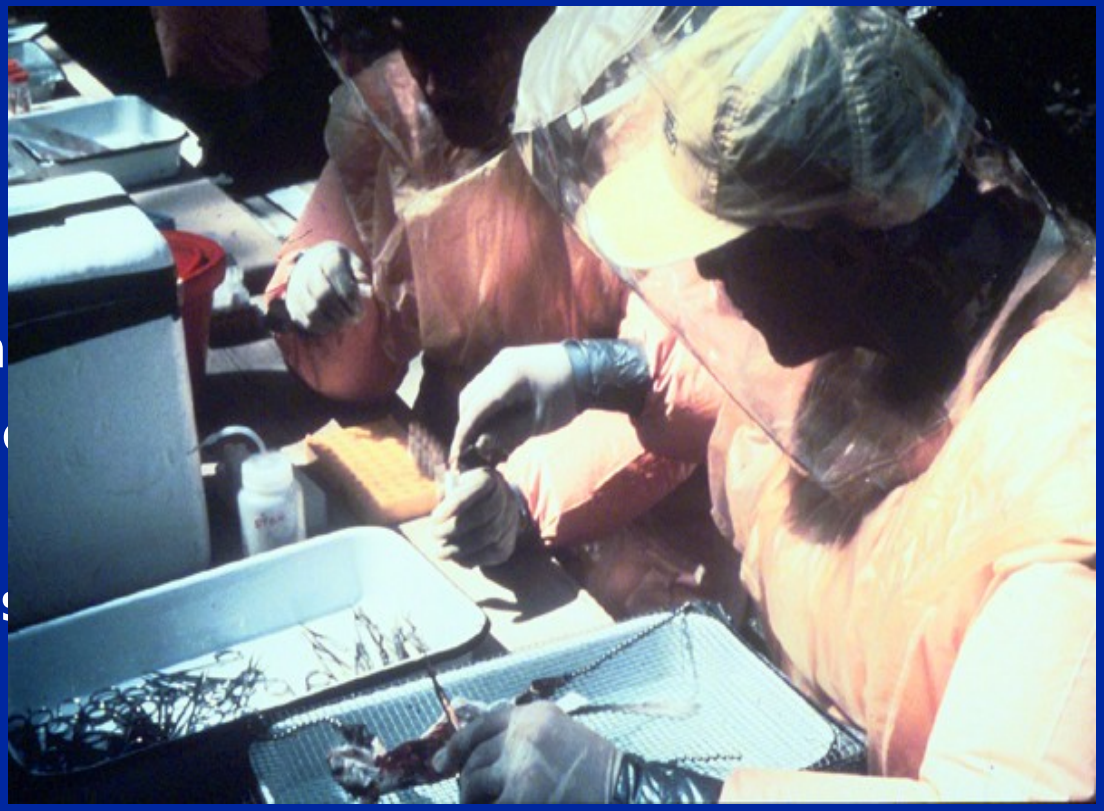


FIGURE 1. Chain of transmission among guests at Hotel M — Hong Kong, 2003
2 family members
Guangdong Province, China
4 family members
2 close contacts
10 HCWs
4 HCWs*
Hospital 2 Hong Kong
Canada
3 HCWs
156 close contacts of HCWs and patients
Hospital 3 Hong Kong
Hotel M Hong Kong
Ireland
United States
99 HCWs (includes 17 medical students)
Hospital 1 Hong Kong
0 HCWs
Hospital 4 Hong Kong
Vietnam
Singapore
HCW
Germany
34 HCWs
37 close contacts
2 family members
28 HCWs
4 other Hong Kong Hospitals
37 HCWs
Unknown number close contacts
Bangkok
* Health-care workers.
† All guests except G and K stayed on the 9th floor of the hotel. Guest G stayed on the 14th floor, and Guest K stayed on the 11th floor.
§ Guests L and M (spouses) were not at Hotel M during the same time as index Guest A but were at the hotel during the same times as Guests G, H, and I, who were ill during this period.

MMWR 2003;52:241-248

Responses to Emerging Diseases

- Microbiology
- Ecology
- Climatology
- Vector biology
- Veterinary medicin
- Population dynami
- Demography
- Behavioral science
- Epidemiology
- Clinical medicine
- Public Health

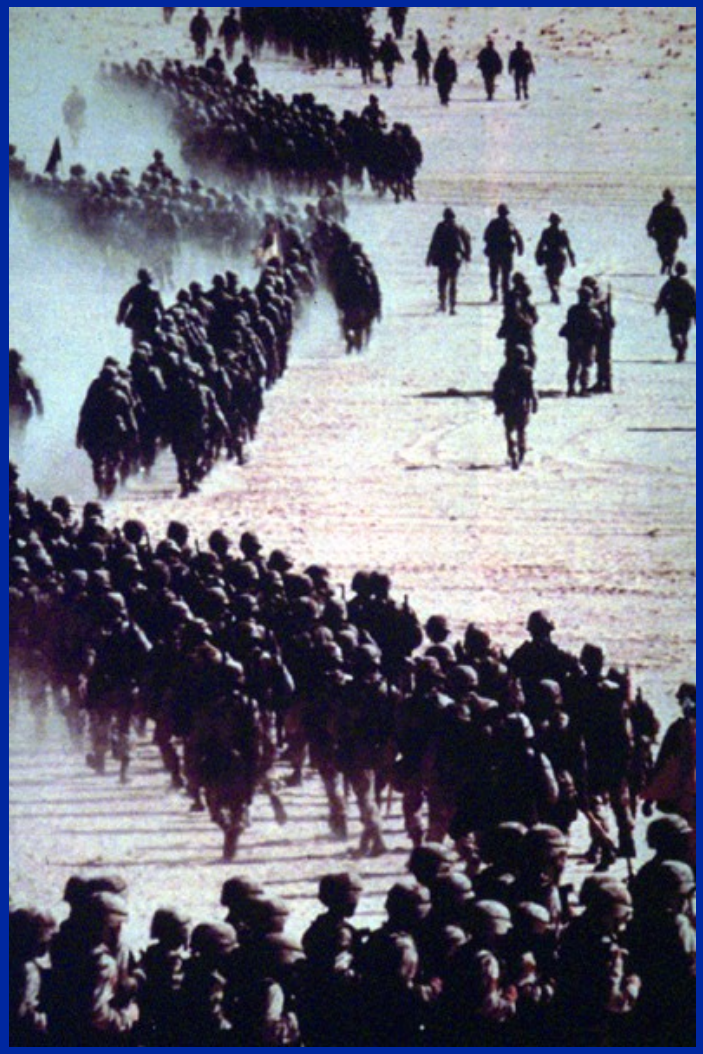


Strategies to Address Emerging Infections

- Detect, investigate and monitor:
  - Emerging pathogens
  - Diseases they cause
  - Factors influencing emergence
- Integrate basic science and epidemiology to optimize public health practice
- Enhance communication regarding public health information
- Strengthen public health system
  - Local, state and federal levels
  - Enhance surveillance
  - Implement prevention/control strategies

– CDC. MMWR 1994;43:RR-5

Military Relevance: Emerging Diseases



- Deployment of immunologically naive population to endemic/epidemic areas
- Proximity to reservoirs/vectors
- Crowding, sanitation/hygiene favor transmission
  - Respiratory
  - Food and water

Military Responses to Emerging Infections

- Preventive medicine environmental assessment capabilities
- Medical surveillance of force (pre/post deployment)
- Training/education of medical personnel on endemic/epidemic diseases
- Field diagnostic and therapeutic capabilities
- Troop education emphasizing prevention
- Immunization/prophylaxis

DoD Global Emerging Infections Surveillance Program

- Facilitate early recognition and control of new diseases affecting military readiness
- Tracking by Overseas Labs
  - Monitor DoD benficiaries
  - Train host-nation epidemiologists
    - Assess and control threats
    - Network with foreign health agencies and WHO
- Monitor drug resistant Plasmodia
- Monitor drug resistant enteric pathogens twice yearly
- Monitor for leptospirosis, yellow fever, dengue, hantaviruses

DoD Global Emerging Infections Surveillance Program

- **Hubs:**
  - **WRAIR/NMRI USAMRIID**
  - **CHPPM**
  - **Armstrong Laboratory**
  - **NHRC-San Diego**
- **Labs:**
  - **Brazil**
  - **Peru**
  - **Egypt**
  - **Kenya**
  - **Thailand**
  - **Indonesia**

A Word of Appreciation…

U.S. Army Medical Research Institute of Infectious Diseases

Armed Forces Institute of Pathology

Centers for Disease Control and Prevention

Bronx Zoo/Wildlife Conservation Society

New York City Public Health Dept

University of New Mexico

World Health Organization